CHEST Online Supplement

Critically Ill Adults With Coronavirus Disease 2019 in New Orleans and Care With an Evidence-Based Protocol

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e-Appendix 1.

Supplemental Methods

A. Pilot Protocol Implementation

As a quality improvement initiative and during the observational period, a group of ICUs within the network implemented a pilot protocol guiding the care of the critically ill adult with COVID-19. The feasibility and effectiveness of this protocol was unknown, therefore implementation occurred as a pilot program in two ICUs during the observational period before expanding to all ICUs.

The protocol offered the following detailed guidance regarding the care of a critically ill adult with COVID-19 and acute respiratory failure:

Non-invasive Positive Pressure Ventilation Prior to Tracheal Intubation

The pilot protocol included a recommendation to use bi-level non-invasive positive pressure ventilation in COVID-19 patients who were 1) unable to maintain SpO2 > 88% on 6 liters oxygen via nasal cannula or with significant respiratory effort despite nasal oxygen 2) without a usual contraindication to NIPPV (shock, ventricular arrythmias, vomiting, inability to protect airway, unresponsiveness). Pressure was delivered using a single circuit non-invasive ventilator (Respironics V60) or a dual-limb closed circuit ventilator (Puritan Bennett 980) via a sealed full-face mask. The sealed mask swivel was connected to a "T piece" equipped with two one way flapper valves 1) to prevent rebreathing of exhaled gas into the ventilator circuit, 2) to require exhaled gas to pass over a viral filter to prevent aerosolization of respiratory droplets, and 3) to provide some back pressure in the circuit for assisting the ventilator in maintaining the set CPAP. Initial CPAP was set to 10 and the additional inspiratory pressure was titrated to achieve a respiratory rate of < 30 or to a level that appeared to significantly improve the work of breathing while being tolerable to the patient.

Care of the Tracheally Intubated Patient

The pilot protocol offered guidance on the following care items: selection of tidal volume, positive end-expiratory pressure, indications and application of prone positioning, intravenous fluid management, and sedation management. Details of this guidance was as follows:

- **Tidal volume selection**

Calculate the patient's predicted body weight and set a tidal volume in the range of 4-6 cc/kg of predicted body weight. If the pH remains less than 7.2, increase the rate as high as 34 breaths per minute. If the pH remains below 7.2, increase the tidal volume to a maximum of 8 cc/kg predicted body weight.

- **Positive end-expiroatry pressure selection**

Use the published high peep "ladder" from the ARDS Network trial comparing high versus low peep.

- **Prone positioning**

After the correct tidal volume and peep are set, if the patient's PaO2/FiO2 remains less than 150 as measured by an arterial blood gas or imputed from the SaO2/FiO2 ratio, begin prone positioning. Recommend 16 hours in the prone position and 8 hours in the supine position. Continue cycles of prone-supine positioning as long as the PaO2/FiO2 remains less than 150 in the supine position.

- **Fluid Management**

If the patient has signs of hypovolemia, initiate balanced crystalloid fluid resuscitation. Otherwise, limit the amount of intravenous volume infused, including from medications. If the patient is on no vasoactive medications or only on low doses of vasoactive medications, administer furosemide. If this does not maintain a net negative or even fluid balance and the patient has worsening hypoxemia, consider some modality of renal replacement therapy.

- **Sedation Management**

If the patient does not require prone positioning, target a light sedation strategy with an opiate to treat pain, if present, and dexmedetomidine to treat agitated delirium, if present. On a daily basis, perform a spontaneous awakening and breathing trial.

Care of the Patient at the Time of Extubation

If the patient passes a spontaneous awakening and breathing trial over 30 minutes, extubate the patient to 6 liters/minute nasal cannula. If the patient passes a spontaneous breathing trial and has a guideline-recommended indication for NIPPV, extubate to NIPPV.

If the patient fails a spontaneous breathing trial, but the failure criteria met is not life-threatening, increase the pressure support and PEEP during the spontaneous breathing trial until the failure criteria improves. Next, extubate the patient to NIPPV to an equivalent amount of support provided via facemask instead of tracheal tube. Attempt to transition off NIPPV at least once daily.

If the patient has significant cardiopulmonary decompensation during a spontaneous breathing trial, return the patient to a controlled mode of ventilation and re-attempt a spontaneous awakening and breathing trial the following day.

e-Table 1. Respiratory Devices Used

Device	Safety Net Hospital SARS CoV-2 + ICU Patients	Network ICUs with Quality Improvement Pilot Protocol Integration	Network ICUs without Quality Improvement Pilot Protocol Integration	P value
Never Required Tracheal Intubation	18 (21%)	14 (25%)	16 (17%)	0.15
Highest Support if Never Tracheally Intubated, No. (%)				0.49
Nasal Cannula	6 (33%)	4 (28%)	7 (43%)	
Venturi Mask	0	0	0	
Non-rebreather Mask	1 (5%)	1 (7%)	1 (6%)	
Heated High Flow Nasal Cannula	2 (11%)	1 (7%)	3 (18%)	
Non-invasive Positive Pressure Ventilation	9 (50%)	8 (57%)	5 (31%)	
Highest Support after Extubation, No. (%)				0.21
Nasal Cannula	5 (13%)	5 (19%)	1 (3%)	
Venturi Mask	0	0	1 (3%)	
Non-rebreather Mask	4 (10%)	2 (7%)	6 (22%)	
Heated High Flow Nasal Cannula	5 (13%)	4 (15%)	3 (11%)	
Non-invasive Positive Pressure Ventilation	23 (62%)	15 (57%)	16 (59%)	

p-value = Mann-Whitney U Test for continuous variables, Chi-square test for categorical variables, and Chi-square test for a trend for categorical variables with more than two groups

e-Table 2. Linear Regression Model for Outcome of Ventilator-free Days

Characteristic	β	95% CI for β	P value
Pilot Protocol Integration	6.01	2.69 - 26.55	0.02
APACHE II Score	-0.32	-0.65 - 0.009	0.05
Age	-0.04	-0.22 - 0.14	0.65
PaO2/FiO2 on ICU Admission	0.006	-0.01 - 0.03	0.6

e-Figure 1. Median Tidal Volume Provided on Each ICU Day

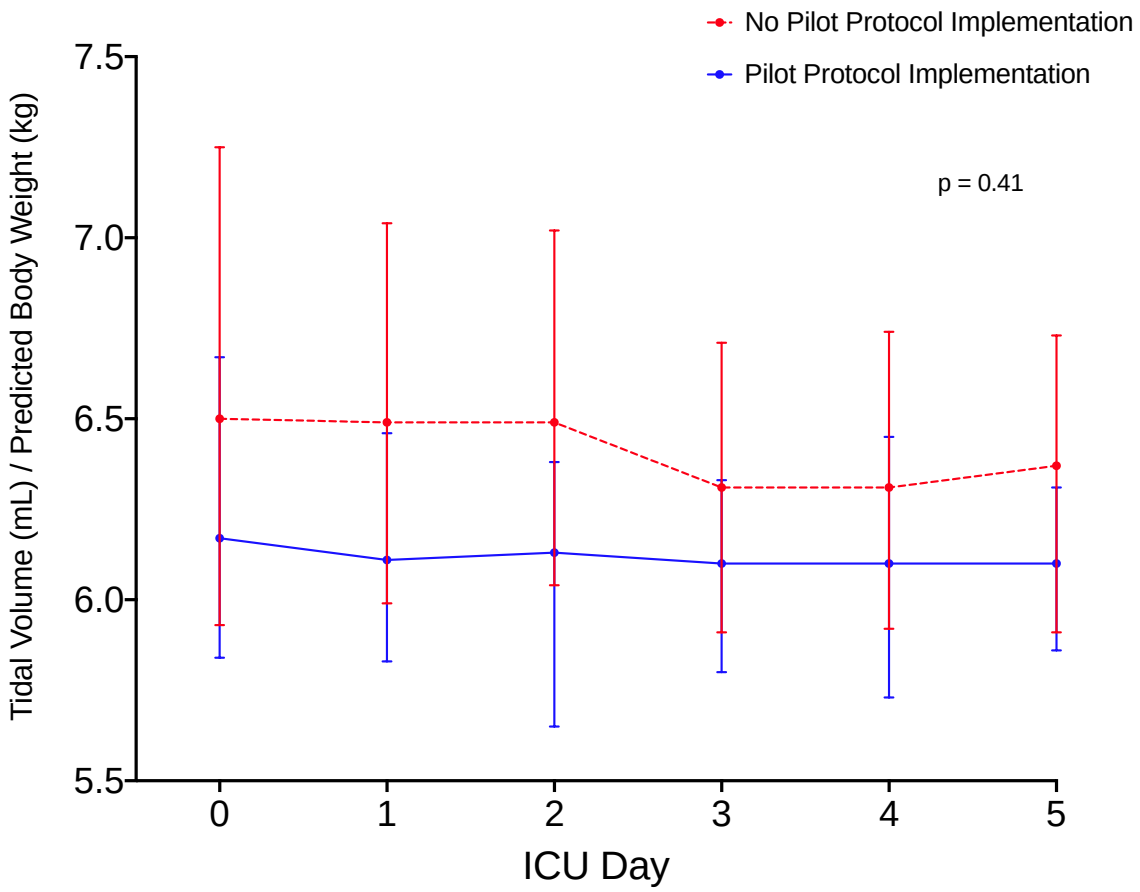

Figure legend: Median values of tidal volume per kilogram of predicted body weight were collected daily for a total of six days. There was no significant difference between groups regarding these repeated measures over time.

e-Figure 2. Median FiO_2/PEEP Ratio provided on Each ICU Day

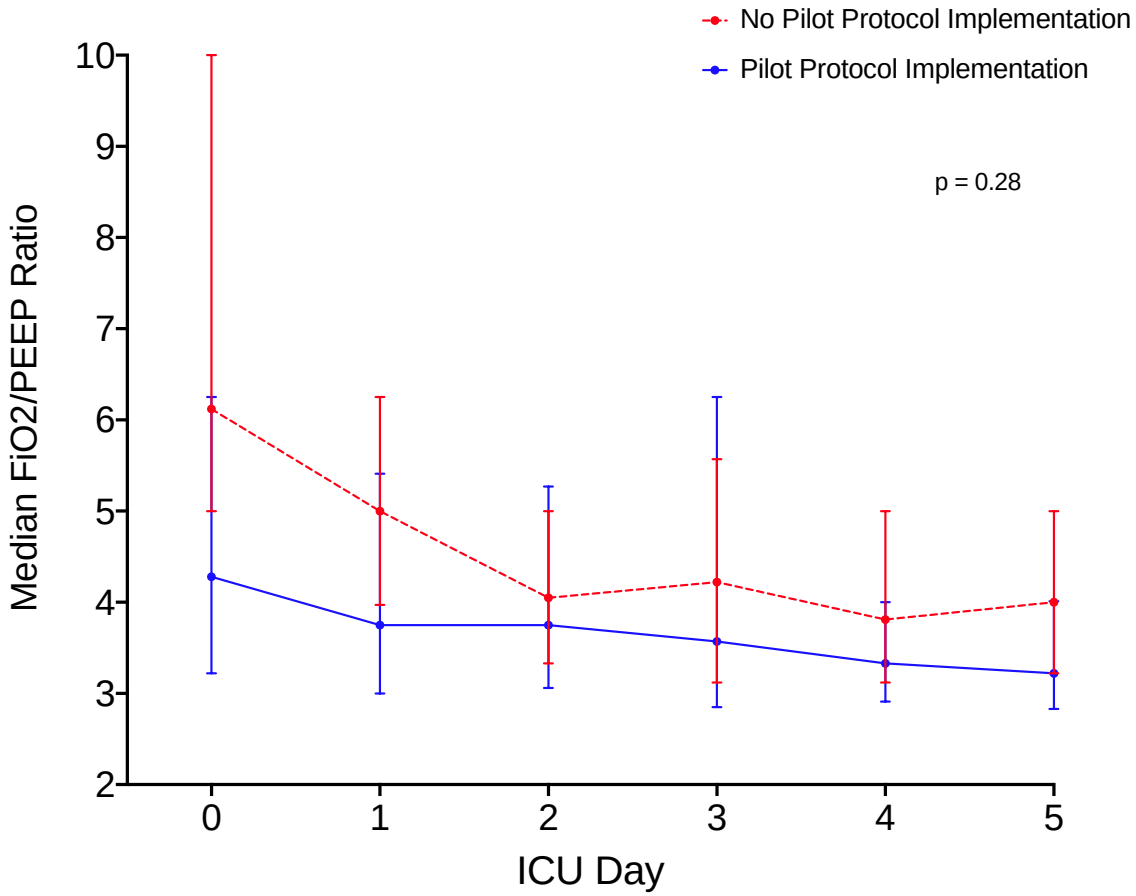

Figure legend: The ratio of percent fraction of inspired oxygen (FiO_2) divided by positive end-expiratory pressure (PEEP) were measured daily in tracheally intubated patients and recorded daily for six days. There was no statistically significant difference between groups regarding this measure over time.

e-Figure 3. Incidence of Prone positioning on Each ICU Day

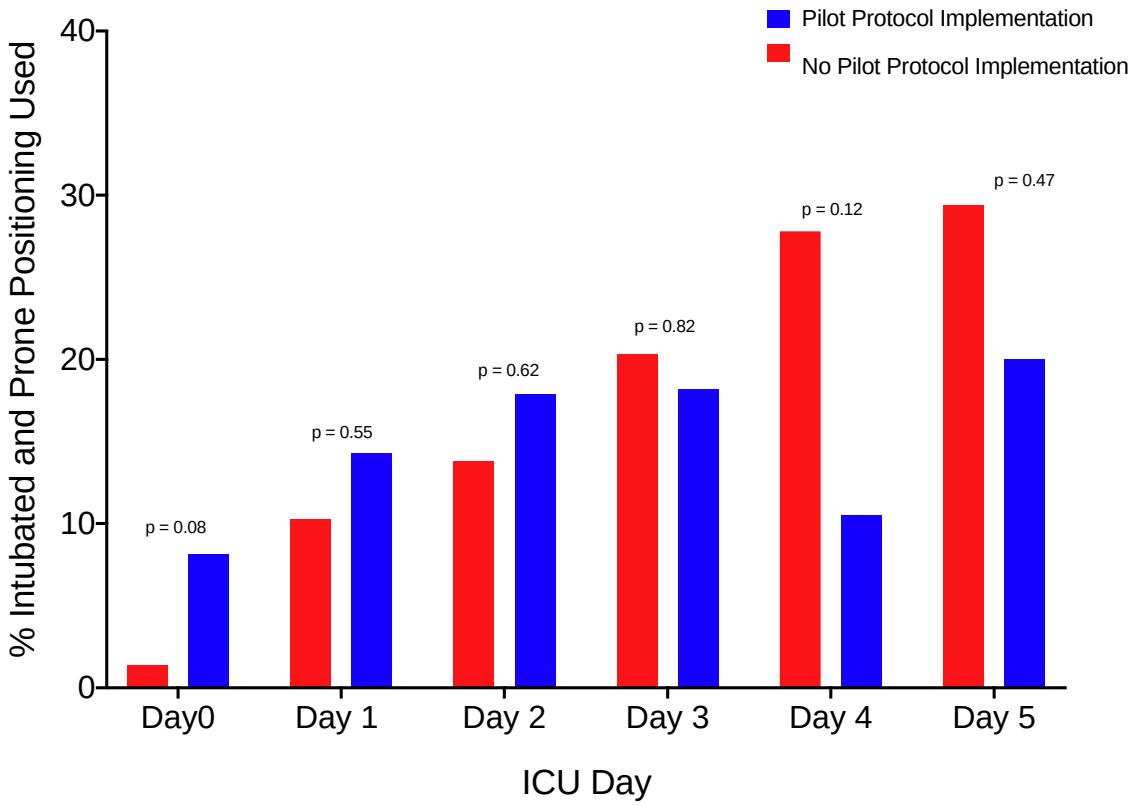

Figure legend: The incidence of prone positioning recorded in tracheally intubated patients and was recorded daily for six days. There was no statistically significant difference between groups regarding this measure on a daily basis.

e-Figure 4. Mean Cumulative Dose of Furosemide administered on Each ICU Day

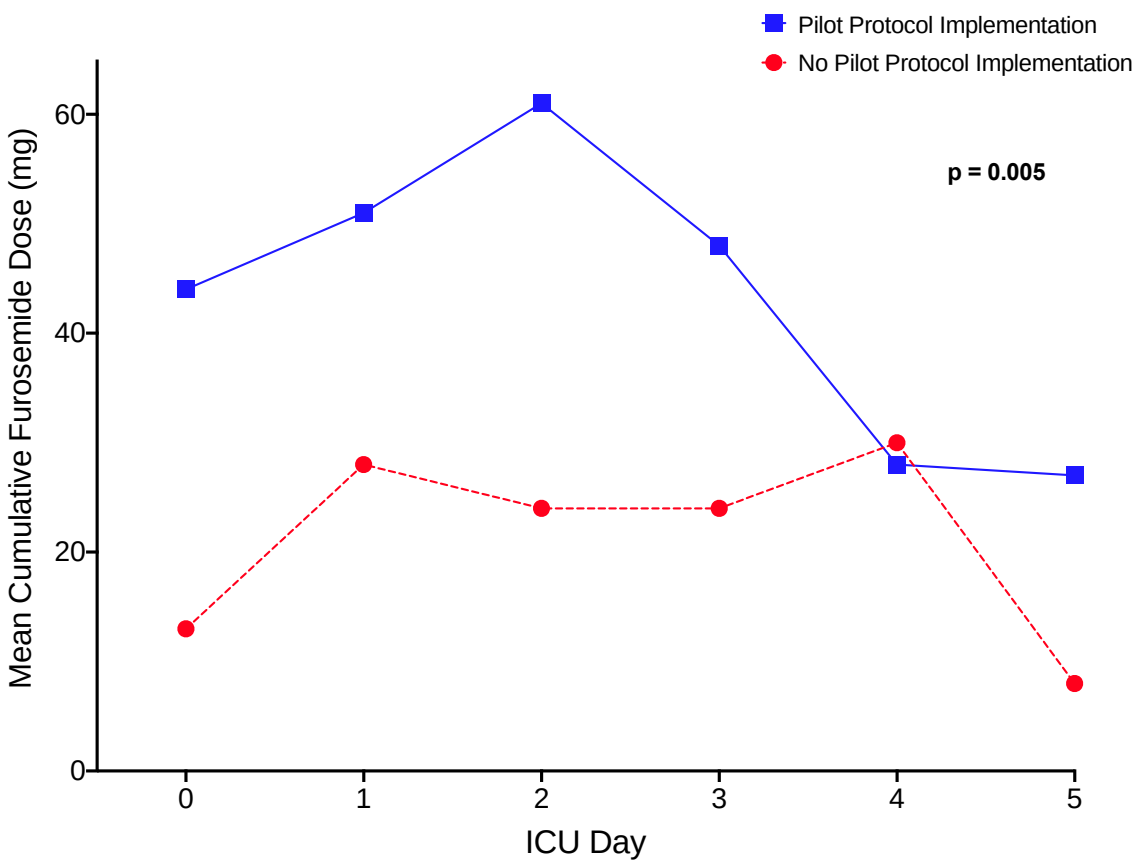

Figure legend: The mean cumulative daily dose of furosemide was calculated and was recorded daily for six days. Pilot protocol implementation was associated with a statistically significant increase in the mean cumulative daily dose of furosemide over time.

e-Figure 5. Ventilator-free days over the course of the observation based on day the patient was admitted

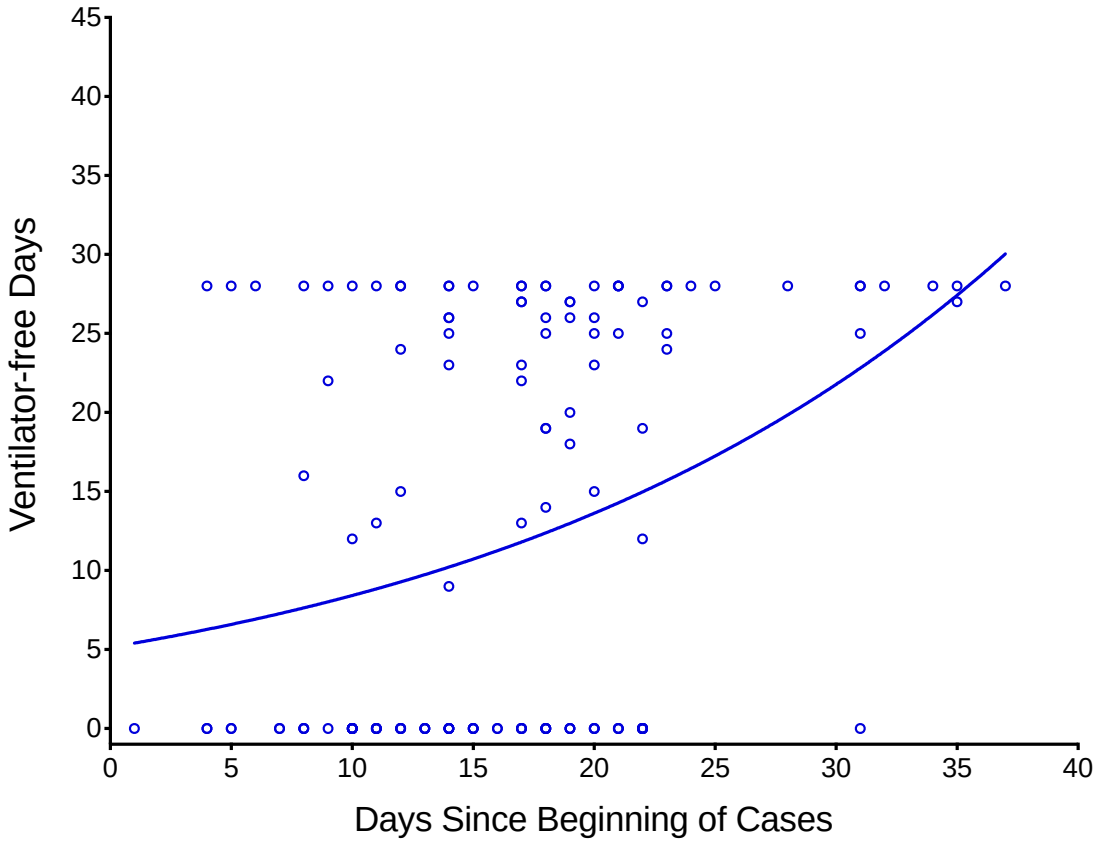

Figure legend: The number of ventilator-free days experienced by each patient based on the date of the patient's ICU admission since the index patient.

e-Figure 6. Ventilator-free days, APACHE II, and SOFA scores over the course of the observation based on day the patient was admitted

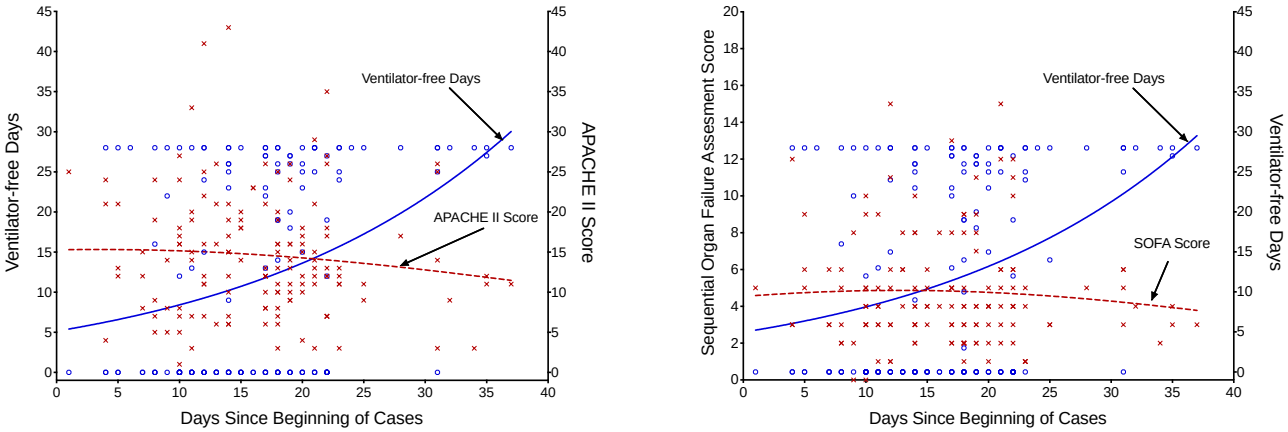

Figure legend: The number of ventilator-free days experienced by each patient based on the date of the patient's ICU admission since the index patient, along with corresponding APACHE II (Panel A) and SOFA scores (Panel B).

e-Figure 7. Ventilator-free days and FiO_2/PEEP ratio over the course of the observation based on day the patient was admitted

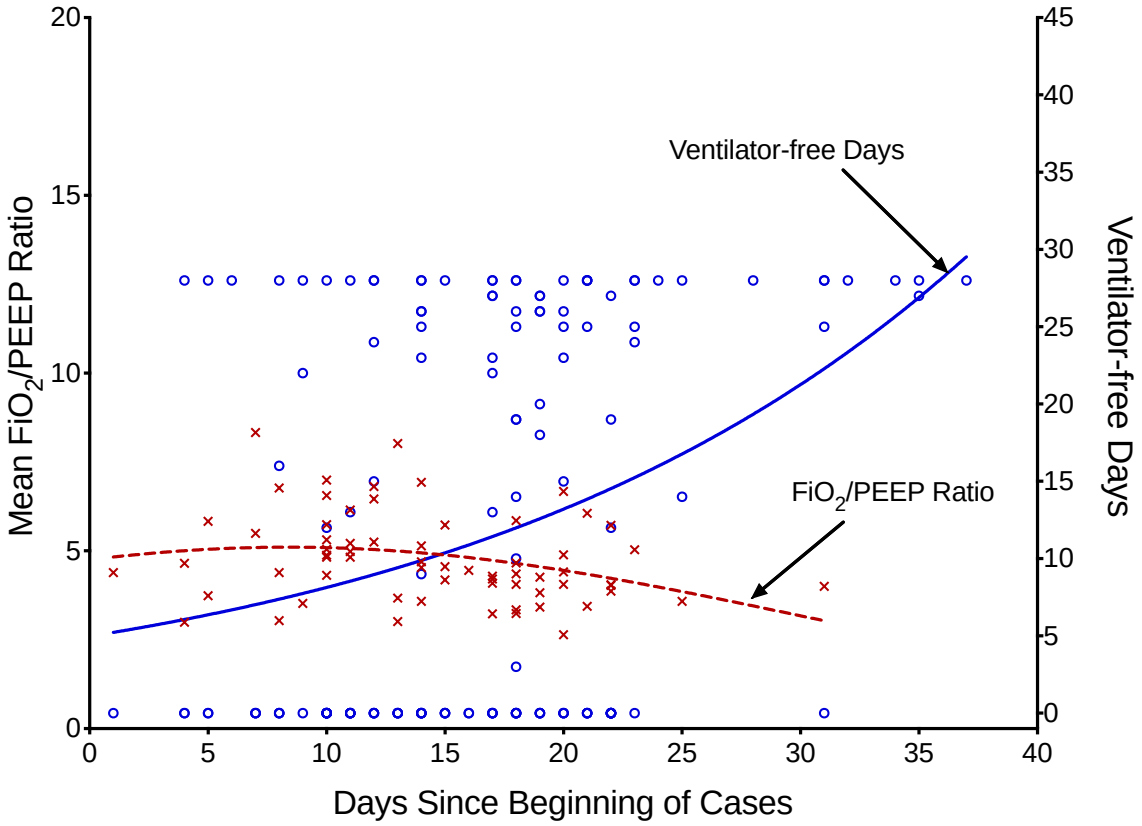

Figure legend: The number of ventilator-free days experienced by each patient based on the date of the patient's ICU admission since the index patient, along with corresponding FiO2/PEEP ratio.

e-Figure 8. Ventilator-free days, mean tidal volume provided during intubation, and mean cumulative furosemide dose administered over the course of the observation based on day the patient was admitted

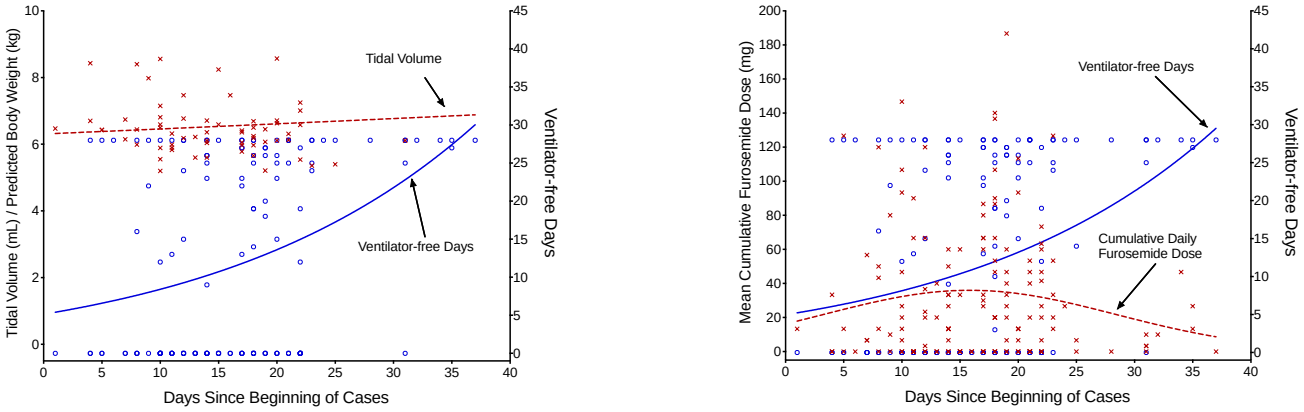

Figure legend: The number of ventilator-free days experienced by each patient based on the date of the patient's ICU admission since the index patient, along with corresponding mean tidal volume provided during tracheal intubation (Panel A) and and mean cumulative furosemide administered (Panel B).